Transcranial optogenetic mapping revealed longitudinal changes in motor maps of ipsi-lesional and contra-lesional cortex following mild traumatic brain injury

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Abstract: Victims of traumatic brain injury (TBI) suffer short- and long-term physical, cognitive, behavioral and emotional impairments that depend on the severity of the injury. Mechanical and cellular alterations in mild TBI can cause global change in inhibition and excitation on the neuronal network level even in the absence of histologically significant cell injury. To understand functional changes of the motor cortex following closed-head mTBI, we applied an optogenetic stimulation method to map motor cortex activity in channelrhodopsins 2 (ChR2) transgenic mice. A closed-head mTBI was performed via a cortical impact device and longitudinal optogenetic mapping of the forelimb areas of the ipsilateral and contralateral motor cortex were done at multiple time points post injury. Optogenetically evoked responses were recorded with electromyography (EMG) in the bicep brachii of the forelimb and with electroencephalography (EEG) in the brain. The mapping revealed immediate suppression of EMG response of the injured ipsilateral motor cortex post mTBI, which was then followed by an enhanced response. The maps also showed a marked increased in the number of responsive spots in the contralateral motor cortex within the first 12 hours. In addition, rotarod behavioral test show a decrease in motor response within first two days after mTBI follows by recovery. In vitro calcium imaging of GCaMP6 cortical slice showed a decrease in intracellular calcium signal at 2 hours post in injury. These data suggest that excitable cortical neurons exhibit short-term impairment locally (epsilateral) as a result of the injury while long-term contralateral hyperexcitability may act as a functional compensatory mechanism. Our data suggests optogenetic mapping of the motor cortex is a valuable technique for longitudinal study of brain functions following mTBI, and that it revealed post-injury hyperexcitability may play an adaptive role in modifying the functional organization of the cortex in response to the short-term activity lost. These longitudinal sequelae may underlie post-traumatic neurological deficits and brain functional recovery.